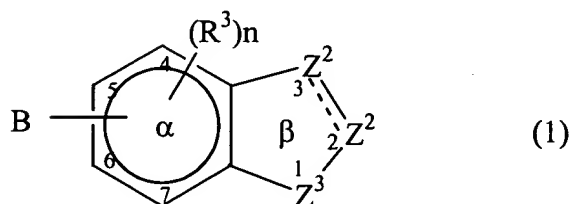


## Abstract

The invention is directed to methods to inhibit p38- $\alpha$  kinase using compounds of the formula



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

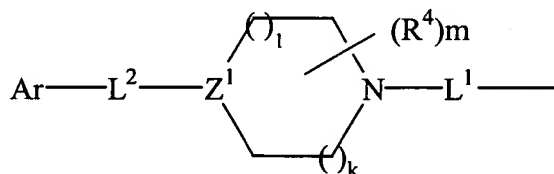
 represents a single or double bond;

B is  $-W_i-CO-X_j-Y$  wherein Y is  $COR^2$  or an isostere thereof and  $R^2$  is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

each R<sup>3</sup> is independently a noninterfering substituent, where n is 0-3;

Z<sup>3</sup> is NR<sup>7</sup> or O; wherein R<sup>7</sup> is H or a noninterfering substituent;

one Z<sup>2</sup> is CA or CR<sup>8</sup>A and the other is CR<sup>1</sup>, CR<sup>1</sup><sub>2</sub>, NR<sup>6</sup> or N wherein each R<sup>1</sup>, R<sup>6</sup> and R<sup>8</sup> is independently hydrogen or noninterfering substituent; wherein A is:



such that Z<sup>1</sup> is CR<sup>5</sup> or N wherein R<sup>5</sup> is hydrogen or a noninterfering substituent;

each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring;

each R<sup>4</sup> is independently a noninterfering substituent where m is 0-4;

each of  $L^1$  and  $L^2$  is a linker; and

the distance between the atom of Ar linked to L<sup>2</sup> and the center of the  $\beta$  ring is 4.5-24Å.